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Gold(I)–Catalyzed Synthesis of Cyclic Sulfamides via an Intramolecular Dehydrative Amination of Allylic Alcohols: A Strategy for 1,3-Diamine Synthesis

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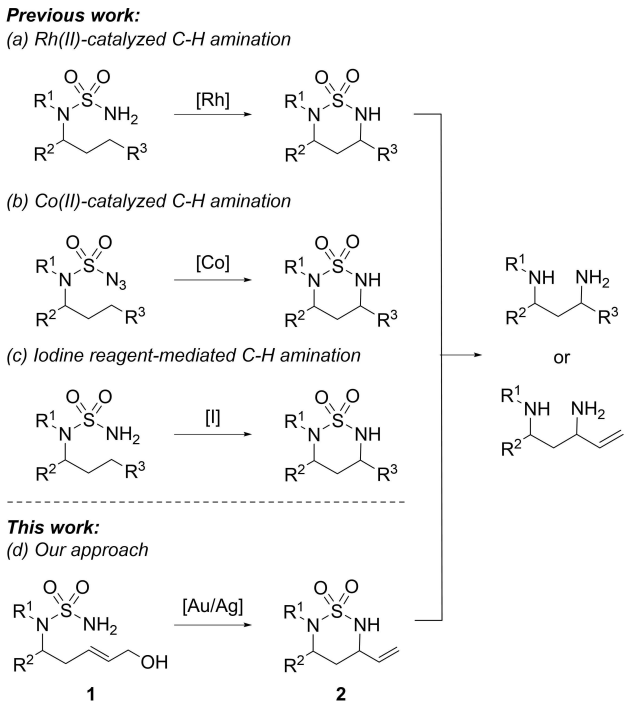
Abstract: A gold(I)-catalyzed intramolecular dehydrative amination method has been developed to synthesize diverse cyclic sulfamides efficiently. Reactions proceed smoothly at room temperature using a combination of (IPr)AuCl (5 mol%) and $AgBF_4$ (5 mol%). This method showcases a broad substrate scope, encompassing challenging seven-membered ring structures, and exhibits functional group compatibility. Moreover, the reaction demonstrates high stereoselectivity, allowing the synthesis of enantiomerically enriched cyclic sulfamides from chiral secondary allylic alcohols. The synthesized cyclic sulfamides serve as valuable intermediates for generating 1,3-diamines. This approach provides an improved route for cyclic sulfamide synthesis and a strategic entry point for obtaining essential 1,3-diamine derivatives.

Keywords: Homogeneous catalysis; Gold; Silver; Amination; Cyclic sulfamide

Cyclic sulfamides represent crucial structural motifs in a broad spectrum of biologically active compounds. These distinctive frameworks are integral to compounds exhibiting diverse pharmacological effects, such as HIV inhibition,[1] serine protease inhibition,[2] modulation of serotonin receptor agonism/antagonism,[3] inhibition of 11β-hydroxysteroid dehydrogenase 1,[4] and antiviral effects.[5] In addition to their biological significance, cyclic sulfamides demonstrate considerable synthetic utility. They have proven effective as chiral auxiliaries in asymmetric aldol reactions,[6] been utilized as nonhydrolyzable peptide surrogates in peptidomimetic design,[7] and acted as precursors for the construction of diverse 1,3-diamine structures.[8]

While cyclic sulfamides have significant pharmacological value and synthetic utility, their synthetic methods remain relatively obscure. Most reported procedures have traditionally involved the reaction of diamines with sulfuryl chloride[9] or sulfamide $H_2NSO_2NH_2$[10] under harsh conditions. Recently, more efficient synthetic approaches for cyclic sulfamides have emerged. Notably, Du Bois et al. demonstrated an elegant cyclization of *N*-Boc-protected sulfamides into corresponding cyclic sulfamides using $[Rh_2(esp)_2]$, along with $PhI(OAc)_2$ and MgO (esp = α,α,α',α'-tetramethyl-1,3-benzenedipropionate) (Scheme 1a).[11] This Rh(II)-catalyzed intramolecular amination exhibited effectiveness for both secondary and tertiary C–H bonds, ensuring stereospecificity and high diastereoselectivity, offering a facile route to synthetically valuable 1,3-diamines. However, the catalytic system proved unsuitable for simple *N*-alkyl sulfamides, which are prone to oxidative degradation by the stoichiometric oxidant $PhI(OAc)_2$.[11] The introduction of an electron-withdrawing group into the substrate mitigated this undesired reaction, with *N*-Boc sulfamides emerging as optimal substrates. Zhang et al. also

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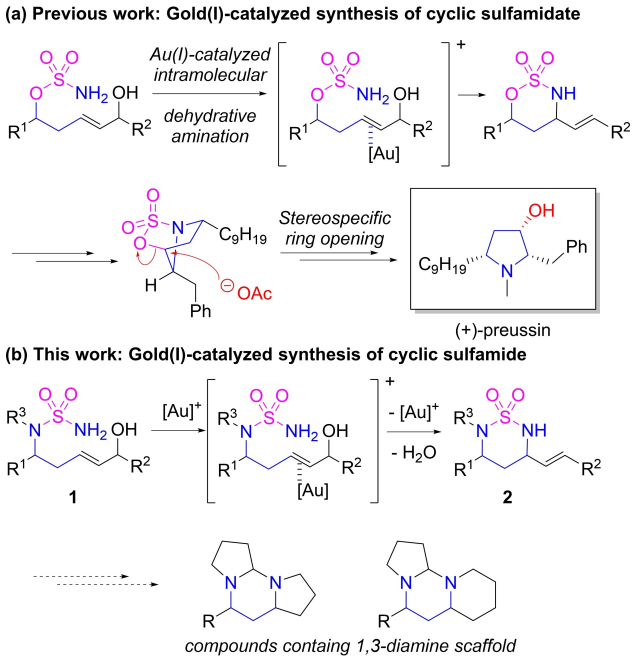
Scheme 1. Strategies for synthesizing cyclic sulfamides and 1,3-diamines.

contributed to the field, presenting a Co(II)-catalyzed intramolecular C–H amination of sulfamoyl azides to yield six-membered cyclic sulfamides, which act as convenient precursors for 1,3-diamine derivatives (Scheme 1b).[12] More recent advancements by various research groups, including those led by Nelson, Marsden, Kiyokawa, and Minakata, have showcased the synthesis of cyclic sulfamides through intramolecular C(sp^3)–H amination of *N*-alkylsulfamides, utilizing iodine-based reagents, as illustrated in Scheme 1c.[13] Despite these notable achievements, a growing need persists for a general and mild catalytic method to synthesize diverse cyclic sulfamides without resorting to oxidants and harsh reaction conditions. In pursuit of this demanding objective, we addressed the issue by employing a gold(I)-catalyzed intramolecular dehydrative amination of sulfamides tethered to allylic alcohols.

Homogenous gold catalysis stands out as a rapidly advancing catalyst research field, proving a potent tool for constructing complex molecules in recent decades. Cationic gold(I) complexes, known for their soft and carbophilic Lewis acid properties, activate C–C π bonds, initiating nucleophilic attacks leading to C–C, C–O, and C–N bond formation. Despite success in activating alkynes, allenes, and terminal alkenes, the activation of internal alkenes by gold has remained largely unexplored.

Allylic alcohols play a pivotal role in our ongoing studies, particularly in intramolecular dehydrative functionalization.[14] The gold(I)-catalyzed intramolecular dehydrative functionalization of allylic alcohols has been extensively explored and meticulously documented with various nucleophiles. Seminal work by Bandini et al. demonstrated gold(I)-catalyzed cyclizations of indoles tethered to allylic alcohols.[15] Independent research by Aponick, Bandini, and Widenhoefer further highlighted the effectiveness of gold(I)-catalyzed intramolecular functionalizations of allylic alcohols, utilizing both alcohol[16] and amine-nucleophiles.[17] Allylic alcohols have proven invaluable as synthetic surrogates for nonactivated alkenes and allenes in these transformations. As part of our ongoing efforts to develop new, efficient synthetic methods for 1,3-diamines, we conceived the idea that gold(I)-mediated activation of internal alkenes, coupled with intramolecular functionalization by sulfamide, could offer an efficient and direct route for synthesizing cyclic sulfamides. This approach provides an alternative to Du Bois's and Zhang's C–H aminations, as illustrated in Scheme 1d. In this context, we present a gold(I)-catalyzed intramolecular dehydrative amination of sulfamide appended to readily accessible allylic alcohols.

In our previous work,[18] we developed a methodology for the synthesis of cyclic sulfamidates via a gold(I)-catalyzed intramolecular dehydrative amination of sulfamate esters tethered to allylic alcohols (Scheme 2a). This strategy provided a convenient and efficient route to access diverse cyclic sulfamidates, which are valuable building blocks due to their broad



Scheme 2. Comparison of gold(I)-catalyzed synthesis of cyclic sulfamidate and cyclic sulfamide.

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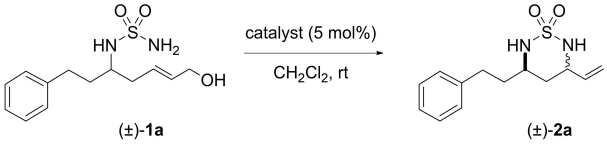
applicability in organic synthesis and medicinal chemistry. Through meticulous experimentation, we successfully applied this method to the stereoselective synthesis of natural product preussin containing 1,3-aminoalcohol scaffold.[19] However, in the pursuit of further advancements in this area, we recognized the potential for extending this methodology to the synthesis of cyclic sulfamides, particularly via the direct intramolecular dehydrative amination of allylic alcohols (Scheme 2b). We believed that the cyclic sulfamides can be used as synthetic intermediates for the stereoselective synthesis of natural products or bioactive compounds containing 1,3-diamine scaffold.

Building upon the success and insights gained from our previous work, we present herein an update to our methodology, focusing on the gold(I)-catalyzed synthesis of cyclic sulfamides as a strategy for 1,3-diamine synthesis (Scheme 2b). This update not only expands the scope of our original concept but also provides an efficient approach for accessing a broader range of nitrogen-containing heterocycles with potential utility in pharmaceutical research. Through a systematic investigation, we aim to demonstrate the efficiency, selectivity, and applicability of this new synthetic route, thus offering synthetic chemists a valuable tool for the synthesis of complex molecules.

In our previous work on the gold(I)-catalyzed synthesis of cyclic sulfamidates,[18] we identified (IPr)AuCl in conjunction with $AgBF_4$ as the most effective catalyst system. Based on this data, we concentrated on the gold and silver catalytic system for the cyclization of allylic alcohol-tethered sulfamide, particularly compound **1a**. Various combinations of gold and silver salts were employed as catalysts in this cyclization process, as detailed in Table 1. Gold catalysts, including (IPr)AuCl and $(PPh_3)AuCl$, were utilized in conjunction with a variety of silver salts such as $AgBF_4$, AgOTf, AgOTs, $AgNTf_2$, $AgSbF_6$, $AgNO_3$, and AgCl. Intramolecular dehydrative cyclizations were carried out at ambient temperature in CH_2Cl_2 as the solvent medium.

Table 1 illustrates that gold(I) salts containing the Cl^- ions, such as (IPr)AuCl (entry 1) and $(PPh_3)AuCl$ (entry 9), exhibited limited effectiveness in promoting intramolecular dehydrative amination reactions. Only trace amounts of the cyclized product **2a** were observed in these cases, even after 48 h. Conversely, a substantial enhancement in yields (91–100%) was achieved when (IPr)AuCl was paired with $AgBF_4$, AgOTf, AgOTs, $AgNTf_2$, $AgSbF_6$, or $AgNO_3$, as indicated in entries 2–7. Notably, the (IPr)AuCl/$AgBF_4$ and (IPr)AuCl/AgOTf combinations facilitated the rapid formation of the cyclized product within 7–8 h (entries 2 and 3), while the (IPr)AuCl catalyst combined with AgOTs, $AgNTf_2$, $AgSbF_6$, or $AgNO_3$ led to comparatively slower reactions requiring 20–48 h (entries 4–7). Nevertheless, the yields in these instances were comparable. Similar trends were observed when $(PPh_3)AuCl$ was combined with $AgBF_4$, AgOTf, AgOTs, $AgNTf_2$, or $AgNO_3$ (entries 10–14).

Table 1. Catalyst screening and optimization of reaction conditions.[a]



entry	catalyst	time (h)	yield (%)[b] (*cis*:*trans*)[c]
1[d]	(IPr)AuCl	48	Trace[d]
2	**(IPr)AuCl/$AgBF_4$**	**8**	**100 (79:21)**
3	(IPr)AuCl/AgOTf	7	95 (74:26)
4	(IPr)AuCl/AgOTs	48	91 (86:14)
5	(IPr)AuCl/$AgNTf_2$	48	100 (76:24)
6	(IPr)AuCl/$AgSbF_6$	20	96 (71:29)
7	(IPr)AuCl/$AgNO_3$	20	98 (77:23)
8	(IPr)AuCl/AgCl	48	trace[d]
9	$(PPh_3)AuCl$	48	trace[d]
10	$(PPh_3)AuCl/AgBF_4$	8	97 (80:20)
11	$(PPh_3)AuCl$/AgOTf	18	94 (74:26)
12	$(PPh_3)AuCl$/AgOTs	48	93 (79:21)
13	$(PPh_3)AuCl/AgNTf_2$	22	98 (69:31)
14	$(PPh_3)AuCl/AgNO_3$	48	37 (78:22)
15	*rac*-BINAP$(AuCl)_2$[f]/$AgBF_4$	24	92 (84:16)
16	*rac*-BINAP$(AuCl)_2$[f]/AgOTs	48	95 (85:15)
17	$AgBF_4$	48	trace[d,e]
18	AgOTf	48	trace[d,e]
19	AgOTs	48	trace[d,e]
20	$NaAuCl_4$	48	trace[d]
21	$NaAuCl_4/AgBF_4$	48	trace[d]

[a] Reaction conditions: **1a** (300 µmol), gold catalyst (15.0 µmol), silver catalyst (15.0 µmol), CH_2Cl_2 (3.0 mL).
[b] Isolated yields after column chromatography.
[c] The diastereomeric ratio is based on ^1H NMR.
[d] Starting material was recovered.
[e] The reaction was performed at 50 °C.
[f] 5 mol% Au was used.

Interestingly, the (IPr)AuCl/AgCl combination failed to yield the desired product (entry 8). This outcome substantially reinforces the proposition that the impact of counteranions[20] on the cyclization process was substantial. The method was also effective with the bidentate phosphine ligand BINAP, as highlighted in entries 15 and 16. In contrast, utilizing Ag salts such as $AgBF_4$, AgOTf, or AgOTs as the sole catalyst, as seen in entries 17–19, proved ineffective, resulting in only traces of the product after 48 h at 50 °C. Therefore, the remarkable reactivity of the (IPr)AuCl/$AgBF_4$ system must stem from the intrinsic activity of the gold(I) catalyst and its anions.

We also investigated the reaction using the gold(III) catalyst $NaAuCl_4$. The cyclization reaction was carried

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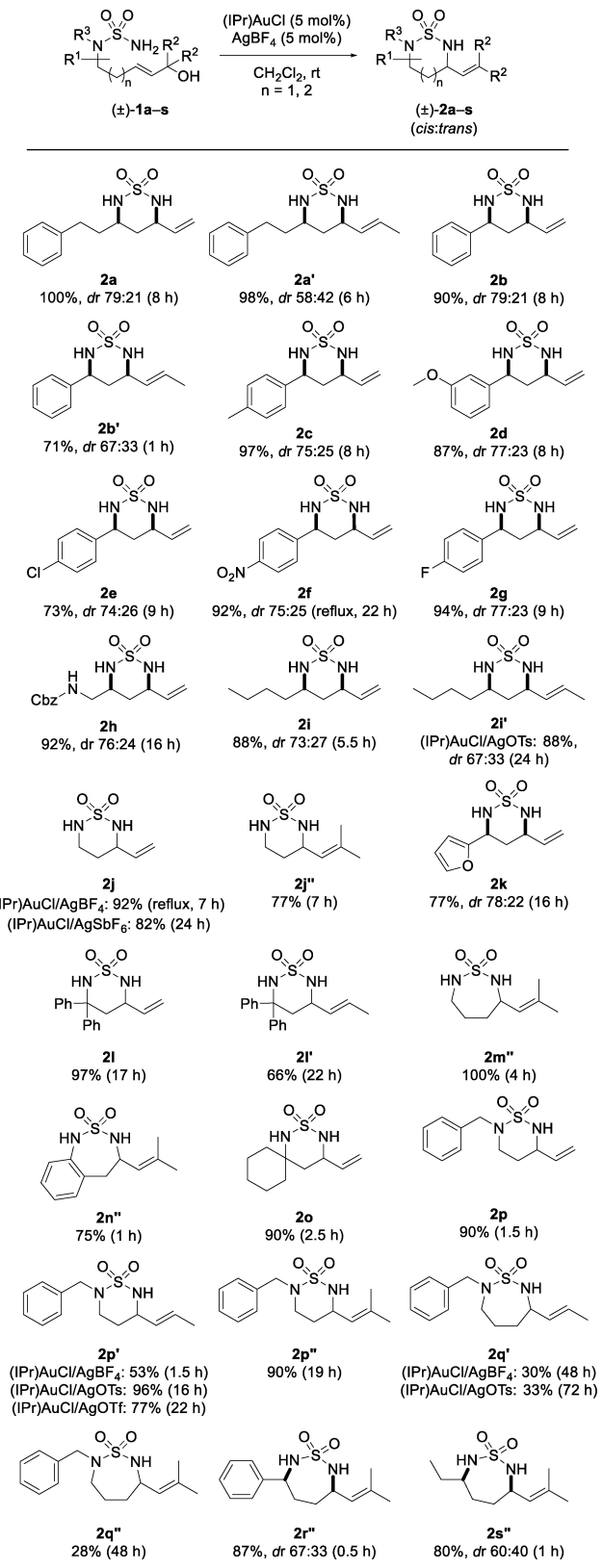
out with $NaAuCl_4$ both with and without $AgBF_4$ under the same conditions as those described in Table 1. Unfortunately, the reaction did not proceed under these conditions (entries 20 and 21).

Our systematic investigation aimed at optimizing reaction conditions identified the most efficient catalytic system using (IPr)AuCl in conjunction with $AgBF_4$. This combination demonstrated remarkable efficacy in facilitating the intramolecular dehydrative amination reaction of a sulfamide tethered to an allylic alcohol. The desired cyclic sulfamide **2 a** was obtained in quantitative yield after a concise 8 h reaction period (entry 2). Additionally, the highest *cis*:*trans* selectivity (86:14) was achieved in the reaction using (IPr)AuCl/AgOTs as a catalyst (entry 4).

After confirming the optimal intramolecular dehydrative amination of allylic alcohol-tethered sulfamide substrate **1 a** with the (IPr)AuCl/$AgBF_4$ combination, we explored the scope of these transformations. Scheme 3 illustrates that these reactions can be performed with electron-rich, -neutral, and -poor allylic alcohol-tethered sulfamides, showcasing good functional group compatibility, including methoxy, fluoro, chloro, nitro, and CBZ-protecting groups. The substrates were synthesized from diverse aldehydes through α-aminoallylation[21] in methanolic ammonia using allylboronic acid pinacol ester, followed by sulfamoylation with a Burgess-type reagent[22] and olefin cross-metathesis employing a Hoveyda–Grubbs 2nd generation catalyst (see supporting information).

The reaction's synthetic efficacy across a diverse range of substrates, demonstrating its broad applicability, was showcased. Initially, phenethyl-substituted sulfamides **1 a** and **1 a′**, along with phenyl-substituted sulfamides **1 b** and **1 b′**, underwent catalytic cyclization, yielding the corresponding cyclic sulfamides **2 a**, **2 a′**, **2 b**, and **2 b′** respectively in good to excellent yields (71–100%) at room temperature within 1–8 h. Electron-rich phenyl-substituted substrates **1 c** and **1 d** exhibited excellent reactivity, producing the desired cyclic sulfamides **2 c** and **2 d** in high yields (87–97%) under mild conditions. Electron-poor phenyl-substituted substrates (**1 e – g**) were also amenable to this transformation, yielding products **2 e – g** in excellent yields (73–94%). Importantly, the scope of the reaction extended beyond phenyl-substituted sulfamides. Alkyl-substituted sulfamides **1 h**, **1 i**, and **1 i′**, nonsubstituted sulfamides **1 j** and **1 j″**, heteroaryl-substituted sulfamide **1 k**, bisphenyl-substituted sulfamides **1 l** and **1 l′**, benzofused sulfamise **1 n″**, bisalkyl-substituted sulfamide **1 o**, and *N*-benzyl-substituted sulfamides **1 p**, **1 p′**, and **1 p″** efficiently underwent cyclization at room temperature.

The formation of seven-membered rings through intramolecular hydroamination catalyzed by transition metals presents a notable challenge because of unfavorable enthalpic and entropic factors.[23] Despite exten-



[a] Reaction conditions: **1** (300 μmol), (IPr)AuCl (9.3 mg, 15 μmol), $AgBF_4$ (2.9 mg, 15 μmol) or Ag salts (15 μmol), CH_2Cl_2 (3.0 mL). Diastereomeric ratio based on ^1H NMR.

Scheme 3. Synthesis of cyclic sulfamides through an Au(I)-catalyzed intramolecular cyclization reaction.[a]

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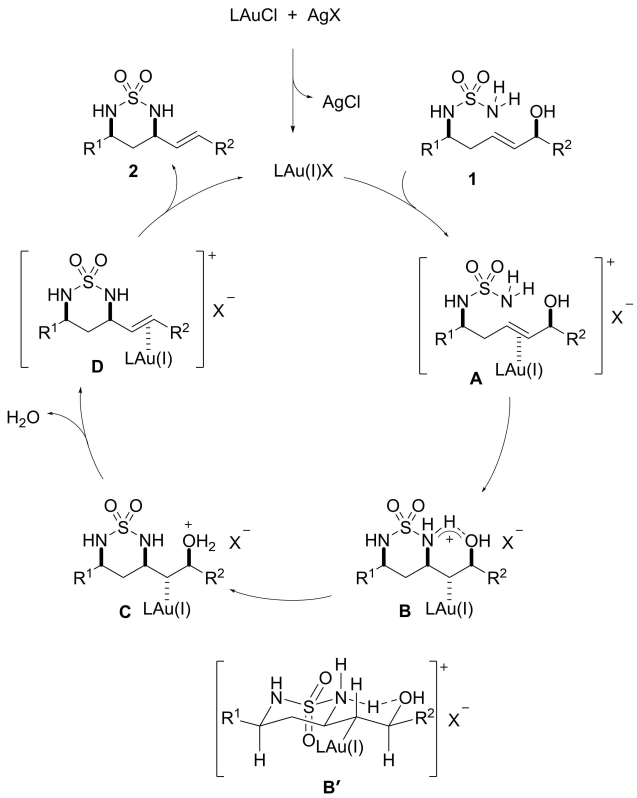
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sive investigations into gold(I)-catalyzed intramolecular hydroamination of alkenes, allenes, and alkynes, the formation of seven-membered rings is a rare occurrence, typically observed only with alkyne substrates predisposed to cyclization.[24] Intriguingly, our approach demonstrated effectiveness in the synthesis of seven-membered sulfamides. The reaction could be readily adapted for the formation of seven-membered ring systems, yielding compounds **2 m″**, **2 n″**, **2 r″**, and **2 s″** with minimal yield loss. However, *N*-benzyl-substituted substrates **1 q′** and **1 q″** exhibited reduced reactivity, resulting in diminished yields (30% and 28%) of the corresponding seven-membered cyclic sulfamides **2 q′** and **2 q″**.

We also investigated the impact of allylic alcohol substitution patterns on the reaction outcome. Both secondary allylic alcohol substrates (**1 a′**, **1 b′**, **1 i′**, **1 l′**, and **1 p′**) and tertiary allylic alcohol substrates (**1 j″**, **1 m″**, **1 n″**, **1 p″**, **1 r″**, and **1 s″**) displayed robust reactivity, yielding the cyclized products in good yields (66–100%), except *N*-benzyl-substituted substrates **1 q′** and **1 q″**, which exhibited lower yields in the context of seven-membered ring cyclization. These findings underscore the versatility and synthetic utility of the catalytic cyclization method across a wide range of substrates, paving the way for diverse applications in organic synthesis.

In line with prior investigations[16c,17,25] and our empirical findings,[18] we present a plausible mechanistic pathway depicted in Scheme 4. The pathway initiates with the coordination of π-acidic cationic gold(I) species[26] to the olefinic moiety of compound **1**, forming metal-π-alkene complex **A**. Intramolecular cyclization proceeds through an anti-addition mechanism, forming hydrogen-bonded metal–alkyl complex **B**. Upon proton transfer to the hydroxyl group, intermediate **C** is generated. Following this step, anti-elimination of water occurs, leading to the formation of cyclic sulfamide **2** through the creation of metal-π-alkene complex **D**. This proposed mechanistic sequence finds substantial support in prior studies,[16c,17,25] which have outlined an analogous anti-addition/anti-elimination pathway for the gold(I)-catalyzed intramolecular functionalization of allylic alcohols. Nevertheless, the intricate details of this mechanism and the potential involvement of silver remain to be elucidated.

In previous studies, Aponick[16c] and Widenhoefer[17c] reported the impact of a chiral secondary allylic alcohol moiety on the stereoselectivity of gold(I)-catalyzed allylic amination/alkoxylation reactions. Notably, Widenhoefer et al. postulated the involvement of a hydrogen-bonded decalin-type conformation.[16c] In this study, we explored the influence of secondary allylic alcohol moiety chirality on the stereoselectivity of intramolecular dehydrative amination reactions of allylic alcohol-tethered sulfamides (Scheme 5). Specifically, we examined configurationally defined and enantiomerically enriched allylic alcohol substrates **(+)-1 a′** and **(−)-1 b′**, leading to the formation of *cis*-cyclic sulfamides **(+)-(*R*,*R*)-(*E*)-2 a′** and **(−)-(*S*,*R*)-(*E*)-2 b′**, respectively, as the major products.

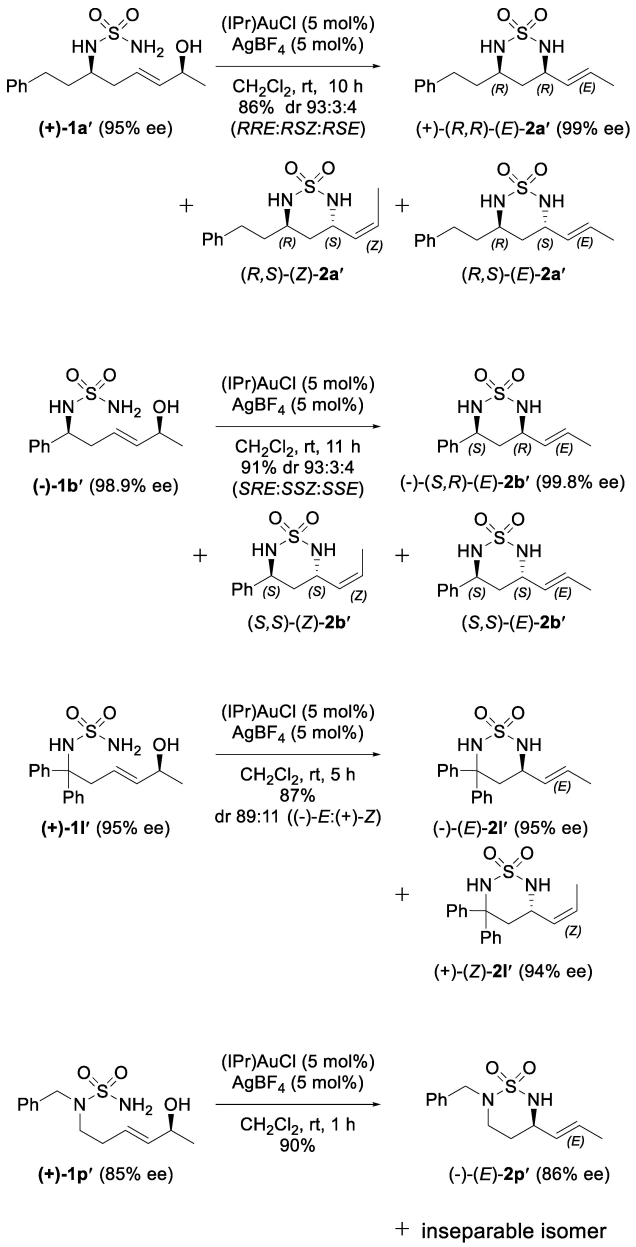


Scheme 4. Plausible mechanism.

The cyclization of **(+)-1 a′** yielded the major product **(+)-(*R*,*R*)-(*E*)-2 a′**, a *cis*-disubstituted cyclic sulfamide, alongside a minor diastereomeric mixture of **(*R*,*S*)-(*Z*)-2 a′** and **(*R*,*S*)-(*E*)-2 a′**, both *trans*-disubstituted cyclic sulfamides, in a diastereomeric ratio of 93:3:4. The major diastereomer **(+)-(*R*,*R*)-(*E*)-2 a′** was successfully separated from the minor diastereomers, which could not be individually separated and were isolated as a mixture. The structures of these diastereomers were confirmed by NMR spectroscopy, including NOE analysis (see Supporting Information). Similarly, the cyclization of **(−)-1 b′** paralleled the reactivity observed for **(+)-1 a′**. The major product, **(−)-(*S*,*R*)-(*E*)-2 b′**, a *cis*-disubstituted cyclic sulfamide, was separated from the minor diastereomeric mixture of **(*S*,*S*)-(*Z*)-2 b′** and **(*S*,*S*)-(*E*)-2 b′**, both *trans*-disubstituted cyclic sulfamides. As with the cyclization of **(+)-1 a′**, the minor diastereomers from the cyclization of **(−)-1 b′** could not be individually separated and were isolated as a mixture. The structures of these diastereomers were also confirmed by NMR spectroscopy. Notably, *cis*-disubstituted cyclic sulfamides

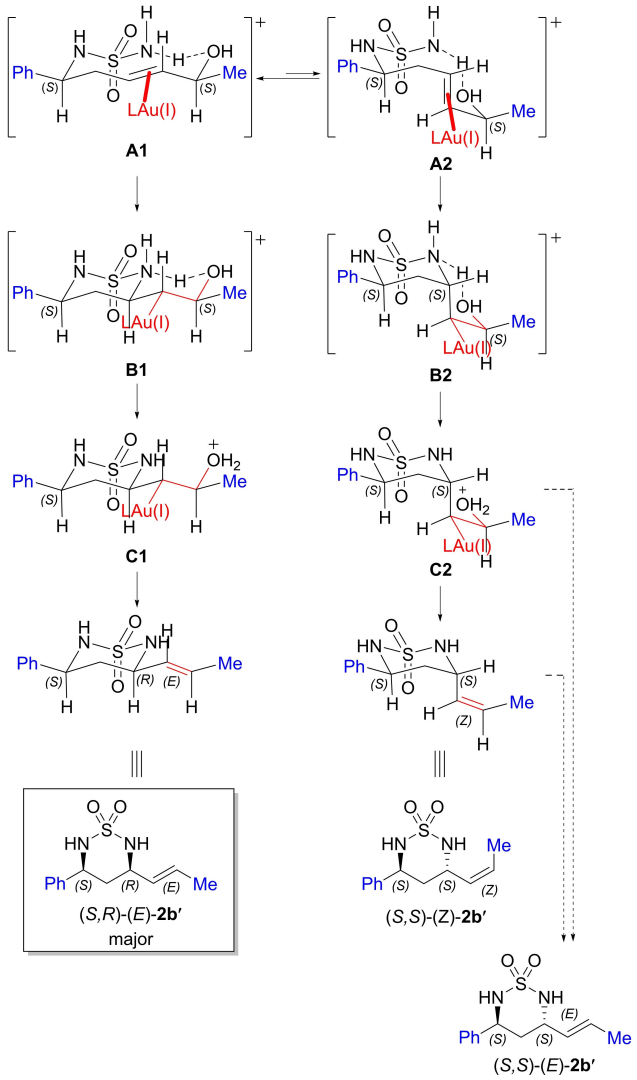
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[a] Reaction conditions: (IPr)AuCl (5 mol%), $AgBF_4$ (5 mol%), CH_2Cl_2 (0.1 M). [b] Diastereomeric ratio based on ^1H NMR.

Scheme 5. Diastereoselective synthesis of cyclic sulfamides through Au(I)-catalyzed stereoselective intramolecular cyclization of chiral secondary allylic alcohols.[a]



Scheme 6. Rationale for the stereoselectivity of the cyclization of **(−)-1 b′**.

with a *Z*-alkene tether were not observed in either reaction.

The observed stereochemical outcome can be rationalized by the decalin-type chair-like conformations **B1** and **B2** (Scheme 6).[16c,17c] π-Activation of the allylic double bond in **(−)-1 b′** can occur on either the *si*-face or *re*-face, leading to the formation of a six-membered chelate structure stabilized by a hydrogen bond between the sulfamide nitrogen and the allylic hydroxyl group. This interaction facilitates nucleophilic addition, generating both the *trans*-decalin chair-like conformation **B1** and the *cis*-decalin chair-like conformation **B2**. However, the presence of an unfavorable 1,3-diaxial interaction within the *cis*-decalin conformation **B2** disfavors this pathway. The subsequent *anti*-elimination pathway explains the formation of the major product, **(−)-(*S*,*R*)-(*E*)-2 b′**, and the minor diastereomer, **(*S*,*S*)-(*Z*)-2 b′**. Interestingly, small amounts of **(*S*,*S*)-(*E*)-2 b′** were also isolated. The formation of this minor component might be attributed to either *Z* to *E* isomerization of a primarily formed *Z*-isomer towards the more stable *E*-isomer, or through an alternative elimination pathway. However, the exact mechanism for the generation of **(*S*,*S*)-(*E*)-2 b′** remains unclear.

Furthermore, this presumption gains additional support from the cyclization of enantiomerically

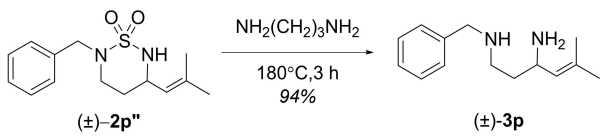
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enriched allylic alcohol substrates **(+)-1 l′** and **(+)-1 p′**, resulting in the production of enantiomerically enriched cyclic sulfamides **(−)-(*E*)-2 l′** and **(−)-(*E*)-2 p′** without any substantial erosion of enantiopurity (Scheme 5). The chirality of the secondary allylic alcohol moiety in **(+)-1 l′** proved to be a powerful directing element for 1,3-asymmetric induction during the cyclization step. Cyclization of **(+)-1 l′** delivered the major product **(−)-(*E*)-2 l′** along with a minor diastereomer **(+)-(*Z*)-2 l′** in excellent enantiomeric excesses of 95% and 94%, respectively (Scheme 5). The absolute configuration of the minor diastereomer was determined to be the opposite of the major diastereomer by comparing optical rotations and chiral HPLC analysis performed after individual catalytic hydrogenation of the major and minor components (see Supporting Information). This finding is consistent with the cyclization outcomes of **(+)-1 a′** and **(−)-1 b′**. Moreover, the cyclization of **(+)-1 p′** produced exclusively **(−)-(*E*)-2 p′**, with a trace amount of minor isomer that could not be separated or identified. This outcome further strengthens the argument that the chirality of the secondary allylic alcohol moiety plays a crucial role for diastereoselective cyclization.

To showcase the potential utility of these compounds as viable intermediates for the total synthesis of polycyclic alkaloid natural products, we endeavored to cleave the sulfamide bridge. From various explored methods, we effectively eliminated the SO_2 moiety under neutral conditions in refluxing 1,3-diaminopropane through transamination,[12d] producing 1,3-diamine **(±)-3 p** in a satisfactory yield of 94% (Scheme 7).

In conclusion, we have successfully developed a versatile gold(I)-catalyzed intramolecular dehydrative amination strategy for synthesizing cyclic sulfamides. This method offers a mild and general approach for constructing diverse cyclic sulfamides, including those with challenging seven-membered ring structures. This reaction's broad substrate scope and functional group compatibility make it a valuable tool for synthesizing various cyclic sulfamides with diverse substituents. The versatility of this approach holds promise for creating biologically active compounds, and our ongoing laboratory research is focused on its application to the synthesis of polycyclic alkaloid natural products.



Scheme 7. Ring-opening reaction for the generation of 1,3-diamine.

Experimental Section

To a 15 mL oven-dried round-bottom flask with a side arm were added (IPr)AuCl (9.3 mg, 15.0 μmol, 5 mol%.) and $AgBF_4$ (2.9 mg, 15.0 μmol, 5 mol%) in a glove box. A solution of (*E*)–*N*-(7-hydroxy-1-phenylhept-5-en-3-yl) sulfamide (**1 a**) (85.6 mg, 300 μmol) in anhydrous CH_2Cl_2 (3 mL) was added. The reaction mixture was stirred at room temperature for an indicated time in table 1. Upon completion of the reaction, the reaction mixture was filtered through a plug of Celite® and rinsed with EtOAc (30 mL). The filtrate was concentrated in vacuo and purified by column chromatography (40:1 CH_2Cl_2/EtOAc) to afford *cis* and *trans* cyclic sulfamide **2 a** (79.9 mg, 300 μmol, 100%, *cis*:*trans* 79:21) as a white solid.

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